



# Evaluation of the bone mineral density in the Mexican female population using the Radiofrequency Echographic Multi Spectrometry (REMS) technology

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## Abstract

**Summary** The bone health status of a Mexican female population, including a cohort of 455 women aged over 40 years, was assessed by Radiofrequency Echographic Multi Spectrometry (REMS).

**Purpose** Assessment of the bone health status in an average female Mexican population with REMS. The secondary objective investigated age- and body mass index (BMI)–related effects on the diagnostic classification and the influence of risk factors for osteoporosis.

**Methods** Women aged over 40 years underwent a REMS scan at the lumbar spine and both femoral necks. The degree of correlation of the bone mineral density (BMD) across axial sites was assessed by the Pearson correlation coefficient ( $r$ ), along with the diagnostic discordance. The association between risk factors, age, and BMI and diagnostic classification was determined by the chi-squared test.

**Results** Four hundred seventy-one women were enrolled. Osteoporosis was diagnosed in 11.0%, 8.1%, and 8.3% of cases at the lumbar spine and right and left femoral neck, respectively. The diagnostic agreement between the lumbar spine and femoral necks was about 73% (85% considering a 0.3 T-score tolerance), whereas the agreement between the femoral necks was 97.4% (99.6% considering a 0.3 T-score tolerance). Most of discordant cases were minor discordances. The correlation between the lumbar spine and femoral neck was  $r=0.82$  and  $0.85$ , respectively, whereas both femoral necks correlated with  $r=0.97$ . As expected, the prevalence of osteoporosis increased with age and decreased as BMI increased.

**Conclusion** The widespread applicability of the non-ionizing REMS technology has been demonstrated in a representative Mexican cohort, covering wide age and BMI ranges. Age and BMI variations correlate with the prevalence of osteoporosis, in line with the recent scientific literature.

**Keywords** Osteoporosis diagnosis · Radiofrequency Echographic Multi Spectrometry · Body mass index · Bone health

## Introduction

Osteoporosis is a silent disease characterized by the reduction of bone strength and deterioration of the bone micro-architecture, which culminates in increased bone fragility and subsequent susceptibility to fracture [1]. This disorder is the most common bone mineral disease in the population aged 50 years that worsens with advancing age, especially in women after the menopause. Indeed, it is estimated that

more than 50% of women aged over 70 have an increased risk of fractures that has repercussions on the quality of life, physical disabilities, healthcare costs, and ultimately increased mortality [1, 2]. The lumbar spine and the hip are common anatomical sites frequently predisposed to osteoporotic fractures that are associated to a high mortality rate [3, 4].

Currently, osteoporosis is quantitatively diagnosed as reduced bone mineral density (BMD) using dual-energy X-ray absorptiometry (DXA) [5]. Although DXA is considered the “gold standard” for BMD measurements, it encompasses several important limitations derived by the exposure to X-rays and the related risks, the need for dedicated infrastructures, high costs, large dimensions of the equipment, and the necessity of trained personnel [6].

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Altogether these shortcomings make DXA inadequate for mass population screening. In addition, given that DXA measures the BMD on a projectional image, it does not provide information on the internal bone microarchitecture, which is a determinant feature of bone strength [6, 7]. DXA is an X-ray imaging technique that shares the same principle of X-rays or gamma ray photon attenuation derived by the penetration through the mass of material, with the level of radiation accounting for only 10% that of a normal chest X-ray. In particular, DXA relies on the emission of two types of low-dose X-rays that are differentially absorbed by bone and soft tissues. Differences in the attenuation profiles of X-ray beams, dependent on the thickness and composition of tissues they pass through, allow to evaluate the BMD status. Thus, the lower the bone density, the greater the risk of fracture. The obtained measurement is expressed as the standard deviation from a healthy reference population, denoted as *T*-score, thereby comparing the BMD of the individual under examination to that of a population at peak bone mass [6]. However, the obtained BMD value is corrupted by a combination of measurements derived by interposed tissues other than bone, including bone marrow, adipose tissue, and others nearby [7]. Consequently, DXA is affected by poor accuracy and repeatability with precision errors in the range of 1 to 2% [8]. Additional factors that limit the actual effectiveness of DXA include errors in patient positioning, image segmentation, and result acquisition [9, 10].

At present, a non-invasive Radiofrequency Echographic Multi Spectrometry (REMS) technology has been developed [11]. This device is based on the use of ultrasounds that through a convex transducer operating at 3.5 MHz central frequency enables the assessment of the BMD on the central reference sites, including the lumbar vertebrae and proximal femur [12, 13]. This technology offers information on the bone health status, thanks to two innovative clinical parameters, namely the BMD and the fragility score (FS). The first is directly related to the bone mineral density estimation, while the second grades the skeletal fragility independently from the BMD, further allowing the qualitative evaluation of the bone microarchitecture [14]. This technology exploits the features of the whole spectrum of radiofrequency (RF) signals acquired during an echographic scan, comparing the obtained spectrum with spectral reference models, in order to determine not only the BMD but also the status of internal bone architecture. In addition, one of the most relevant advantages of REMS is represented by the capacity to recognize artifacts, such as calcifications and osteophytes, and to automatically discard them from the analysis [15]. The acquisition is rapid, taking overall 4 min at both the lumbar and femoral regions. Furthermore, the utilization of REMS does not require the necessity for any particular equipment, as it is a portable instrument. Overall these advantages

denote a beneficial impact of REMS on the patient management as well as on current diagnostic protocols [11].

When REMS was compared to DXA for the diagnosis of osteoporosis, the diagnostic sensitivity of REMS was found to be 91.5% for the femoral neck and 91.7% for the lumbar spine, whereas the diagnostic specificity was 91.8% and 92.0%, respectively. By evaluating the diagnostic concordance between DXA and REMS, when the three categories of the WHO classification (healthy, osteopenia, osteoporosis) were considered, REMS showed a high diagnostic correlation with the gold standard, reaching 88.2% for the femoral neck and 88.8% for the lumbar spine. Furthermore, eliminating borderline effects by applying a 0.3 *T*-score tolerance threshold, the diagnostic agreement increased to 98.0% and 97.4%, respectively. Nevertheless, the authors emphasize the importance of a rigorous training of the operators in order to avoid improper measurements and to improve the diagnostic accuracy of REMS acquisitions [16].

Hence, with this study we aim to assess the bone health status in an average female Mexican population using REMS. The secondary objective of the study evaluates age- and BMI-related effects on the diagnostic classification of bone status and the influence of risk factors associated to the development of osteoporosis.

## Methods

### Data collection

An observational, transversal, and descriptive study was conducted at the UMAE, Hospital de Gineco Obstetricia No. 4 “Luis Castelazo Ayala” of the Mexican Institute of Social Security (IMSS). A total female population of 455 women aged over 40 years (of whom 78.0% were aged under 60 years) was enrolled in October 2018 and spontaneously underwent a bone evaluation. Furthermore, the ethical approval was obtained to conduct the study. The hospital is a third level of care, which in 2018 granted 95,629 specialty consultations and had 12,819 births of which 6269 were by cesarean section, and 11,688 gynecological surgeries of which 10,320 were for benign pathology and 1368 oncological. Despite the variety of services that the Unit provides, it does not have its own densitometry equipment. So, an agreement was established within the IMSS network for the use of the REMS device (EchoStation, Echolight S.p.A., Lecce, Italy) at the hospital of Gineco Obstetricia No. 4. All REMS acquisitions at the lumbar spine and both femoral necks were carried out by the same operator. In order to evaluate the potential risk factors associated to the BMD loss, data were collected from each participant by means of a questionnaire and recorded in the case report form, for which a template is shown in Supplementary Information S1.

## Statistical analysis

The diagnostic classification was performed independently for the scanned anatomical sites and the used threshold values were in accordance with the standards recommended by the World Health Organization (WHO): each scan resulted in a classification of “osteoporosis” if *T*-score was less than or equal to  $-2.5$ , “osteopenia” if *T*-score was between  $-2.5$  and  $-1.0$ , or “healthy” if *T*-score was equal or greater than  $-1.0$  [17]. The diagnostic agreement between two anatomical sites was assessed as the percentage of corresponding cases classified in the same diagnostic category. Moreover, the diagnostic agreement was also evaluated accepting a 0.3 tolerance on *T*-score value of borderline cases around the threshold values of  $-2.5$  and  $-1$ , as already performed in previous studies [16]. The degree of correlation between BMD values assessed at different anatomical sites was quantified by the Pearson correlation coefficient (*r*), the coefficient of determination ( $r^2$ ), and the standard error of estimate (SEE).

The patient’s characteristics were evaluated as median values and interquartile ranges (IQR). The relationships between the prevalence of risk factors for osteoporosis and patients’ diagnosis were investigated with the chi-squared test. Moreover, a logistic regression analysis was performed between the diagnostic classifications in two classes (“osteoporotic” if the *T*-score value was less than or equal to  $-2.5$  or “non-osteoporotic” if the *T*-score value was greater than  $-2.5$ ): the resulting odds ratio (OR) represented the increased likelihood of having a diagnosis for osteoporosis in the presence of a given risk factor than in absence of that risk factor. A multiple logistic regression analysis was also performed incorporating all factors resulting statistically significant at the previous logistic regression.

Age- and BMI-related prevalence of WHO categories (healthy, with osteopenia, with osteoporosis) was investigated by the chi-squared test for significance, by stratifying the population in respective age and BMI categories. With respect to the stratification by age, all patients were subdivided into nine 5-year groups (i.e., 40–44 years, 45–49 years, etc.). Thus, the significance was tested from a contingency table of nine (variables for age) by three (variables for healthy, with osteopenia, with osteoporosis). Regarding the BMI distribution, the patients were categorized into three groups in agreement with the WHO classification [18]: *normal weight* if BMI was equal to or greater than  $18.5 \text{ kg/m}^2$  and less than  $25.0 \text{ kg/m}^2$ ; *overweight* (or *pre-obese*) if BMI was equal to or greater than  $25.0 \text{ kg/m}^2$  and less than  $30.0 \text{ kg/m}^2$ ; *obese* if BMI was equal to or greater than  $30.0 \text{ kg/m}^2$ . Analogously, the significance was tested from a contingency table of three (variables for BMI) by three (variables for healthy, with osteopenia, with osteoporosis).

**Table 1** Demographic data of the population under investigation. *BMI*, body mass index; *IQR*, interquartile range

Demographic data	
Enrolled patients	471
Cohort assessed in the study	455
Ethnicity	Hispanic
Median age (years)	52 (range: 40–87) (IQR: 47–58)
Median height (cm)	156 (range: 135 to 180 cm) (IQR: 152–160)
Median weight (kg)	68 (range: 38–122) (IQR: 60–76)
Median BMI ( $\text{kg/m}^2$ )	27.7 (range: 16.8–48.3) (IQR: 24.8 to 30.9)
Normal (%)	27.9
Pre-obese (%)	40.9
Obese (%)	31.2

**Table 2** Diagnostic classification by anatomical site

	Lumbar spine	Right femoral neck	Left femoral neck
Healthy	131 (29.8%)	231 (50.8%)	226 (49.7%)
Osteopenia	274 (60.2%)	187 (41.1%)	191 (42.0%)
Osteoporosis	50 (11.0%)	37 (8.1%)	38 (8.3%)

## Results

### Baseline characteristics

A total of 471 patients were included in this study, 16 of which were excluded from the analysis because of incomplete data on risk factors or densitometry reports, thus resulting in a cohort of 455 women. Demographic data of the study population are shown in Table 1. The data are expressed as median values and both the range and IQR values are indicated.

### WHO-based diagnostic classification

Osteoporosis was diagnosed in 11.0% of cases at the lumbar spine, 8.1% of cases at the right femoral neck, and 8.3% of cases at the left femoral neck. The results concerning the diagnostic classification at different anatomical sites are reported in Table 2. The diagnostic agreement between the lumbar spine and left femoral neck was 73.6% (85.5% when a 0.3 *T*-score tolerance was considered), whereas between the lumbar spine and right femoral neck, the agreement reached 72.7% (84.6% considering a 0.3 *T*-score tolerance). The diagnostic concordance increased to 97.4% (99.6% considering a 0.3 *T*-score tolerance) between left and right femoral necks. Considering the discordant cases, the large majority were minor discordances. The latter are associated

to adjacent diagnostic classes; for instance, a patient was classified as normal for one axial site and osteopenic for the other site or as osteopenic for one site and osteoporotic for the other site. In particular, 26.2% and 27.0% were minor discordances existing between the lumbar spine and left/right femoral neck, whereas discordances between the right and left femoral neck resulted to be only 2.0%. A major discordance, i.e., a classification as healthy in one site and osteoporotic in the other site, has been observed only for one case (0.4%), both between the lumbar spine ( $T$ -score value =  $-2.5$ ) and femoral necks ( $T$ -score values  $-1.0$  and  $-0.9$  for the left and right femoral neck, respectively).

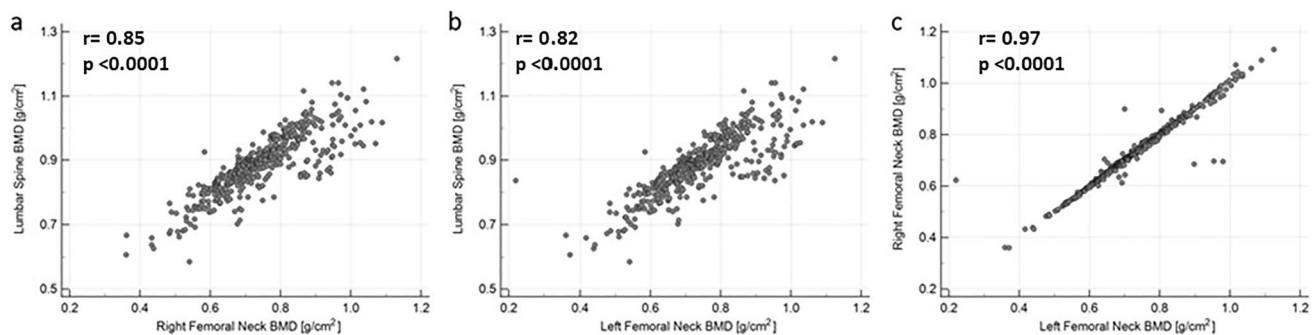
### Correlation of BMD assessed at different anatomical sites

The analysis of the correlation between lumbar spine BMD and left and right femoral neck BMD resulted in a Person correlation coefficient  $r=0.82$ , ( $r^2=0.68$ , SEE =  $0.052 \text{ g/cm}^2$ ) and  $r=0.85$  ( $r^2=0.72$ , SEE =  $0.049 \text{ g/cm}^2$ ), respectively, whereas  $r=0.97$  ( $r^2=0.94$ , SEE =  $0.031 \text{ g/cm}^2$ ) was

observed between BMD values measured at left and right femoral necks (Fig. 1).

### Analysis of risk factors for osteoporosis

Potential risk factors associated to the development of osteoporosis included the following variables: ongoing medication, tabagism, parental osteoporotic fracture, secondary osteoporosis, rheumatoid arthritis diagnosis, use of glucocorticoids, history of osteoporotic fractures, and alcoholism. A chi-squared test was carried out to investigate the relationship between the above factors and the  $T$ -score values assessed at the lumbar spine and both femoral necks, with  $p$  values highlighted in bold when a significant effect was observed (Table 3). Overall, medication, rheumatoid arthritis diagnosis, and previous history of osteoporotic fracture appeared to be significantly associated to an increased risk of osteoporosis at all axial sites, whereas parental osteoporotic fractures significantly correlated with the lumbar spine only.



**Fig. 1** Scatterplot of the BMD values assessed at different anatomical sites. The panels show the correlation (Person correlation coefficient  $r$ ) and  $p$  values between the BMD values measured at **a** the right

femoral neck versus the lumbar spine; **b** the left femoral neck versus the lumbar spine; and **c** the left femoral neck versus the right femoral neck

**Table 3** Risk factors for osteoporosis reported as absolute and relative prevalence. The association between the risk factors and osteoporosis diagnosis is investigated with the chi-square test and resulting  $p$  values are included, with statistically significant values highlighted in bold

Risk factor	Count (%)	Lumbar spine $p$ value	Right femoral neck $p$ value	Left femoral neck $p$ value
Ongoing medication *	138 (30.2)	<b>&lt;0.0001</b>	<b>0.0003</b>	<b>0.0001</b>
Tabagism	78 (17.1)	0.85	0.16	0.08
Parental osteoporotic fracture	62 (13.6)	<b>0.0065</b>	0.61	0.74
Secondary osteoporosis	23 (5.1)	0.97	0.68	0.40
Diagnosis of rheumatoid arthritis	21 (4.6)	<b>0.0128</b>	<b>0.0153</b>	<b>0.0203</b>
Use of glucocorticoids	17 (3.7)	0.41	0.93	0.70
History of osteoporotic fractures	16 (3.5)	<b>0.004</b>	<b>0.0067</b>	<b>0.0088</b>
Alcoholism	0 (0)	-	-	-

\*Ongoing medication included 22 anti-hypertensive drugs, 21 anti-diabetes drugs, 14 anti-hyperthyroidism drugs, 2 anti-hyperthyroidism therapy and anti-hypertensive drugs, 7 anti-diabetes and anti-hypertensive drugs, 5 estrogen therapy, 5 nonsteroidal anti-inflammatory drugs, 1 QT drug not better specified, 1 anti-asthmatic drug, 1 pain therapy drug and sedative, 1 osteoporosis therapy, 1 contraceptive therapy, 57 not reported

These results were confirmed by the logistic regression analysis, investigating the relationship between the diagnosis of osteoporosis and the presence of a risk factor (Table 4). In particular, the current use of medication was correlated with osteoporosis diagnosed at lumbar spine (OR = 4.53, 95% CI: 2.45 to 8.53,  $p < 0.0001$ ) and with osteoporosis diagnosed at left and right femoral neck sites (for both sites: OR = 3.56, 95% CI: 1.80 to 7.01,  $p = 0.0002$ ); diagnosis of rheumatoid arthritis resulted in an OR of 4.53 (95% CI: 1.74 to 11.85,  $p = 0.002$ ) for osteoporosis diagnosed at the lumbar spine and 3.79 (95% CI: 1.30 to 10.99,  $p = 0.027$ ) at the left and right femoral necks. Moreover, previous history of osteoporotic fractures increased the chance of osteoporosis diagnosed at the lumbar spine (OR = 5.37, 95% CI: 1.86 to 15.49,  $p = 0.0045$ ) and at the left and right femoral necks (OR = 5.58, 95% CI: 1.83 to 17.01,  $p = 0.007$ ). Conversely, current smoking, parental osteoporotic fractures use of glucocorticoids, and presence of secondary osteoporosis were not statistically correlated with the diagnosis of osteoporosis. At multiple logistic regression analysis, the presence of medication and history of osteoporotic fracture were still significantly correlated with the diagnosis of osteoporosis at all anatomical sites.

### Age-related diagnostic classification

The cohort was subdivided by 5-year age groups and classified as “healthy,” “with osteopenia,” or “with osteoporosis” according to the *T*-score (Fig. 2). The diagnostic classification appeared to follow a similar trend among all three axial

sites, with an increased percentage of osteoporotic women in elderly age, in contrast to a higher proportion of healthy women at younger ages. Patients with osteopenia were found to be distributed according to a bell curve shape, reaching the peak between 55 and 64 years old.

A significant relationship between the diagnostic classifications (healthy, with osteopenia, or with osteoporosis) and 5-year age groups ( $p < 0.0001$ ) was predicted by the chi-squared test. This result was confirmed by a negative correlation between BMD values and age assessed by the Pearson correlation coefficient with  $r = -0.69$ ,  $-0.55$ , and  $-0.53$  at the lumbar spine, right femoral neck, and left femoral neck, respectively.

### BMI-related diagnostic classification

Analogously, a similar analysis was performed to evaluate how the diagnostic classification differs according to different BMI groups, including patients with normal weight (only one underweight patient was included in this group), overweight, and obese (Fig. 3). As expected, among obese women the prevalence of healthy increased, concomitantly to a decreased prevalence of osteoporosis. A significant relationship between the diagnostic classification in healthy patients, patients with osteopenia, or patients with osteoporosis and BMI was confirmed by the chi-squared test ( $p < 0.0001$ ). The correlation between BMI and BMD values assessed by the Pearson correlation coefficient  $r$  were 0.49, 0.66, and 0.65 at the lumbar spine, right femoral neck, and left femoral neck, respectively.

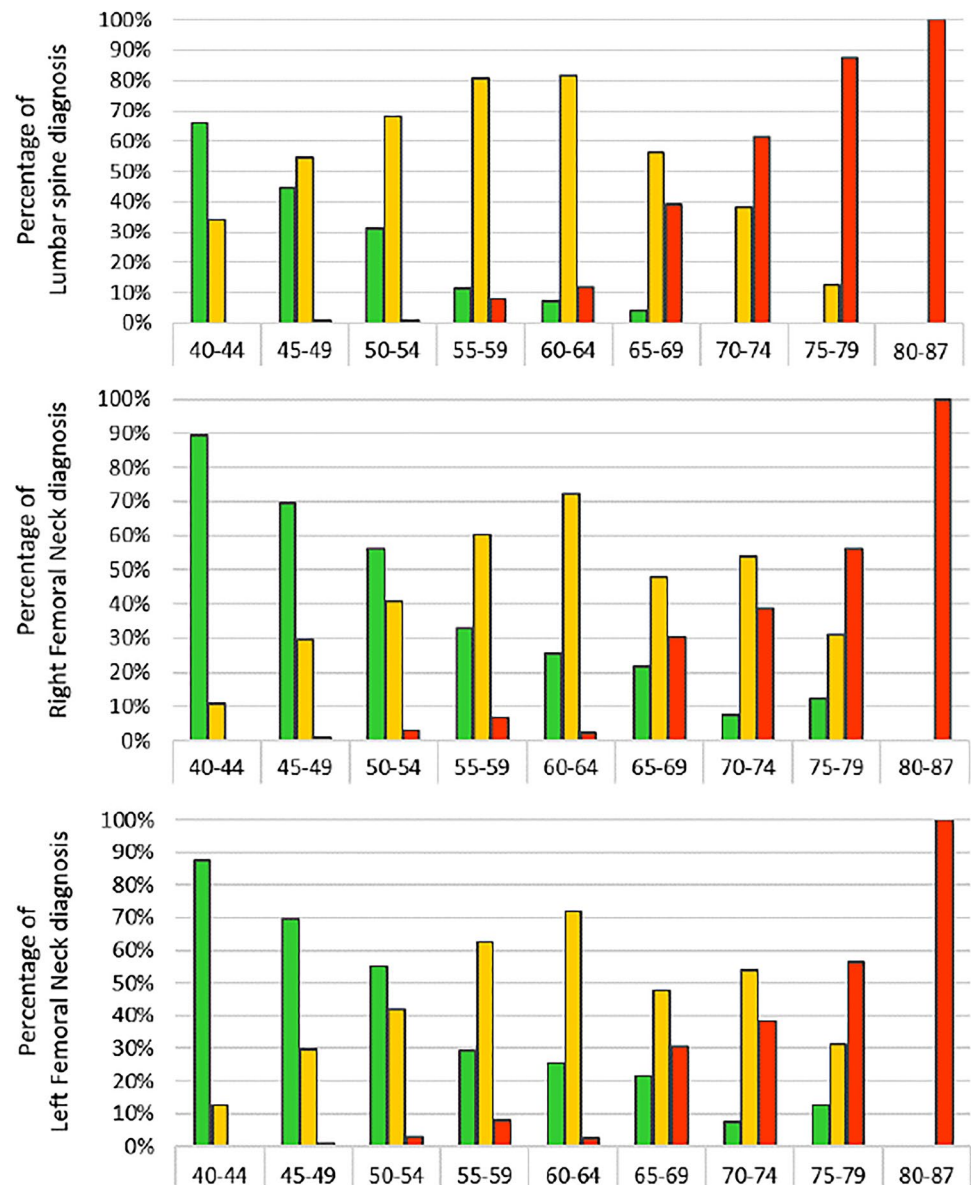
**Table 4** Odds ratio (OR) of risk factors associated to the occurrence of osteoporosis at all reference axial sites. Logistic regression analysis was performed to estimate the OR and resulting *p* values are

included, with statistically significant values highlighted in bold. *CI*, confidence interval; *OR*, odds ratio

Risk factor	Lumbar spine OR (95% CI)	Lumbar spine <i>p</i> value	Right femoral neck OR (95% CI)	Right femoral neck <i>p</i> value	Left femoral neck OR (95% CI)	Left femoral neck <i>p</i> value
Ongoing medication*	4.53 (2.45 to 8.53)	<b>&lt; 0.0001</b>	3.56 (1.80 to 7.01)	<b>0.0002</b>	3.56 (1.80 to 7.01)	<b>0.0002</b>
Tabagism	1.24 (0.59 to 2.59)	0.58	1.83 (0.85 to 3.94)	0.139	1.83 (0.85 to 3.94)	0.139
Parental osteoporotic fracture	1.69 (0.80 to 3.59)	0.19	0.95 (0.36 to 2.54)	0.93	0.95 (0.36 to 2.54)	0.93
Secondary osteoporosis	0.76 (0.17 to 3.34)	0.71	1.37 (0.59 to 3.17)	0.47	1.37 (0.59 to 3.17)	0.47
Diagnosis of rheumatoid arthritis	4.53 (1.74 to 11.85)	<b>0.002</b>	3.79 (1.30 to 10.99)	<b>0.027</b>	3.79 (1.30 to 10.99)	<b>0.027</b>
Use of glucocorticoids	1.71 (0.49 to 6.41)	0.41	1.49 (0.33 to 6.75)	0.62	1.49 (0.33 to 6.75)	0.62
History of osteoporotic fractures	5.37 (1.86 to 15.49)	<b>0.0045</b>	5.58 (1.83 to 17.01)	<b>0.007</b>	5.58 (1.83 to 17.01)	<b>0.007</b>
Alcoholism	-	-	-	-	-	-



**Fig. 2** Distribution of the diagnostic classification by age groups. The percentage of patients including healthy (green bars), with osteopenia (yellow bars), and with osteoporosis (red bars), subdivided by 5-year age groups, resulted from the analysis at the lumbar spine (histogram above), right femoral neck (in the middle), and left femoral neck (below)



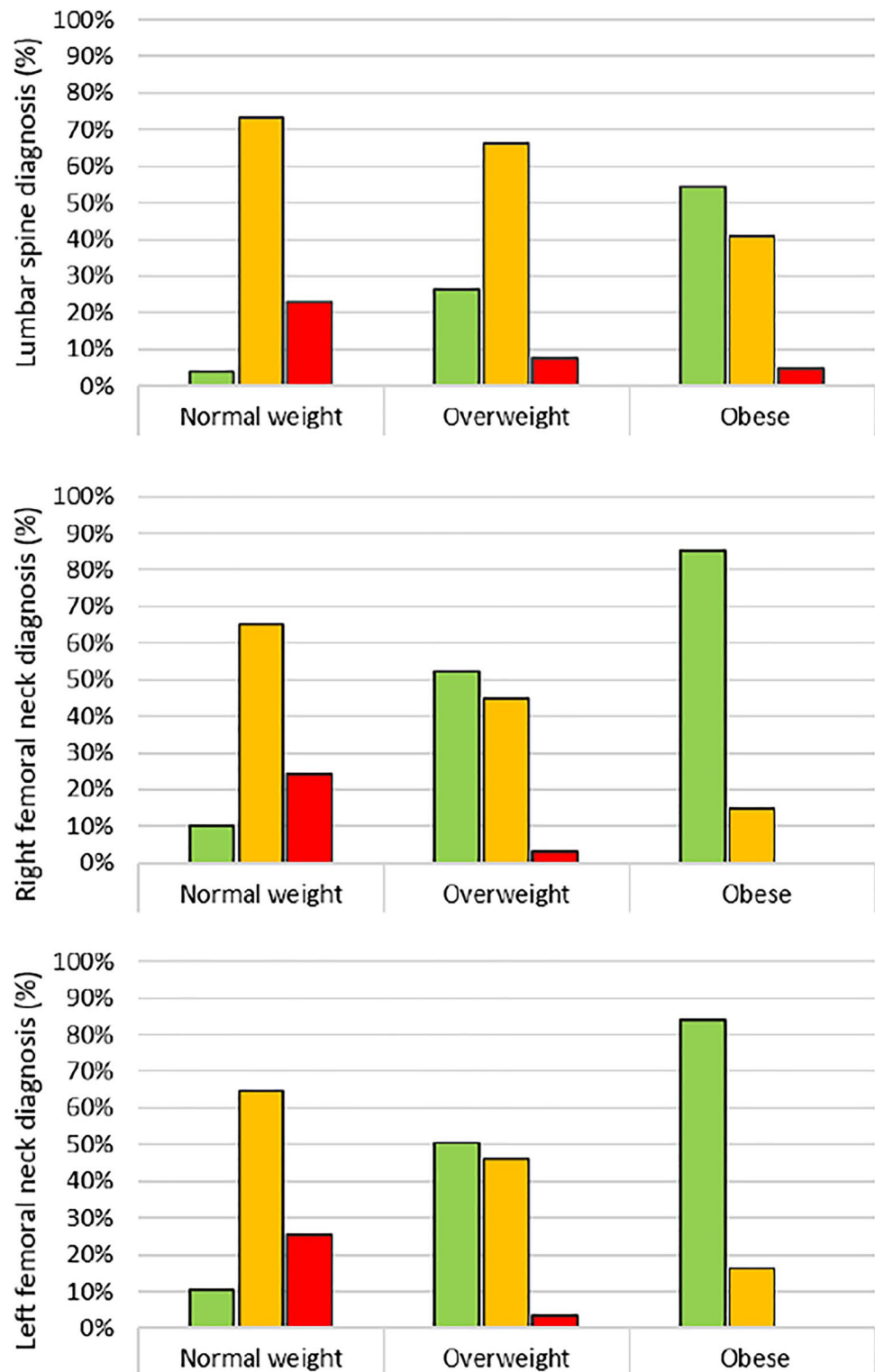
## Discussion

The National Institute of Health in Mexico has recognized osteoporosis as a public health problem [19], with about 17% of Mexican women aged over 50 years diagnosed with osteoporosis in 2010 [20]. In 2018, the economic burden of osteoporosis was estimated to be 411 million USD in Mexico and was the highest among four Latin American countries (namely Brazil, Mexico, Colombia, and Argentina, for which the overall costs accounted for 1.17 billion USD) [21]. Consequently, an effective improvement of the osteoporosis management, prevention, and first-line treatments for individuals at high fracture risk is of paramount importance in Latin America.

In this study, the application of a novel device implementing a non-ionizing approach for the diagnosis of osteoporosis has been presented. Within 1 month, 471 women voluntarily underwent the assessment of bone health status at a rate of about 20 exams a day by REMS. The enrolled women were scanned at the lumbar vertebrae and both femurs. To the best of our knowledge, this is the first study that examines the correlation of the REMS scans performed at different anatomical sites, including both femoral necks.

The characteristics of the enrolled patients were in line with the average Mexican population, for which the prevalence of overweight (i.e., BMI between 25 and 30 kg/m<sup>2</sup>) and obesity (i.e., BMI over 30 kg/m<sup>2</sup>) is reported to be 39.7% and 29.9%, respectively [22]. The applicability of this technology in overweight and obese patients has been already

**Fig. 3** Distribution of the diagnostic classification by BMI groups. The percentage of patients including healthy (green bars), with osteopenia (yellow bars), and with osteoporosis (red bars), according to BMI groups (normal weight, overweight, or obese), resulted from the analysis at the lumbar spine (histogram above), right femoral neck (in the middle), and left femoral neck (below). The underweight class was included in the normal weight group, since only one patient was in this BMI class, reporting osteopenia diagnosis



shown [23, 24] and largely confirmed in this study, with nine enrolled patients presenting an obesity of type III (i.e., BMI greater than 40 kg/m<sup>2</sup>).

The decrease of BMD with age, that in women is due to the drop of estrogens during menopause, is a largely

studied phenomenon [25] that primarily causes bone loss [26]. This effect has also been observed in the current study, demonstrating a negative correlation between BMD and age and, consequently, an age-dependent pattern in the diagnostic classification. A similar trend has been previously

investigated in a large Austrian female population by Boshitsch et al., who found that the rate of patients with osteoporosis progressively augmented in older age groups, accompanied by a simultaneous decrease in the proportion of healthy subjects [27].

In the present study, the correlation between the BMD values measured at the left and right femoral necks was very high, with a Pearson correlation coefficient  $r=0.97$ , in line and even higher than the values that have already been reported using DXA [28, 29].

Moreover, a strong correlation has been observed between the BMD values measured at the femoral necks and lumbar spine (resulting from a Pearson correlation coefficient  $r=0.82$  and  $0.85$  at the left and right femurs, respectively). On the other hand, a relatively higher value of BMD found at the lumbar spine than in femurs is a common tendency in agreement with other studies considering different ethnicities, for instance, Korean subjects [30]. This behavior has also been observed in a representative Mexican female population presented in this study. Indeed, the BMD at the lumbar spine is known to reach the peak at least 5 years before the femur [31]: a generalized lower  $T$ -score value at the lumbar spine, in addition to being more susceptible to develop early osteoporosis, also explains the diagnostic discordances observed between the diagnoses at femurs and spine. Interestingly, in this study, only one case of major discordance has been observed, with borderline  $T$ -score values both at the lumbar spine and femoral necks. The majority of the observed minor discordances were cases with osteopenic lumbar spine and normal femoral necks (95 and 100 cases considering left and right femoral neck, respectively), followed by osteoporotic lumbar spine and osteopenic femoral necks (17 cases for both sides), osteopenic lumbar spine and osteoporotic femoral neck (6 cases for the left side and 5 for the right side), normal lumbar spine, and osteopenic femoral neck (1 case for both sides). The prevalence of these minor discordances is slightly lower than the rate of 30–36% reported in other studies using DXA [32–34]. Of note, the observed minor discordances of diagnosis on different sites were largely due to *borderline cases* that corresponded to a higher or lower 0.3 deviation from the conventional  $T$ -score threshold of  $-2.5$  and  $-1$ . When this  $\pm 0.3$  tolerance, defined as such by Di Paola et al. [16], was accepted before labeling a case as wrong classification, the diagnostic concordance increased up to about 85% between the lumbar spine and femoral necks and 99.6% between the left and right femoral necks.

As expected, the diagnostic classification is worse in patients with a previously diagnosed rheumatoid arthritis, which is often correlated with a diagnosis of osteoporosis [23, 35] or a history of osteoporotic fractures [36, 37]. Interestingly, an association between the presence of parental fragility fracture and reduced BMD assessed at the lumbar

spine was observed, confirming the heritability of low BMD as already thoroughly studied [35, 38, 39]. Furthermore, also several classes of medications represented a relevant risk factor for developing osteoporosis. Most of the commonly prescribed medications have a direct impact on the bone turnover and metabolism, thus perturbing the BMD levels and increasing the vulnerability to fracture risk [40].

A number of limitations of this study need to be acknowledged. First, the study population was recruited from a single institution and involved women only. However, the lead institute, fully dedicated to women's health, is one of the largest centers conducting BMD measurements at multiple sites in Mexico. Further studies involving men and adolescents are advised. Second, this observational study recruited a mixed cohort including women with and without a prescription for a BMD examination. A bias on the diagnostic classification might be introduced by the patients with a medical prescription because they may have a higher likelihood of being affected by osteoporosis than the general population. However, the proportion of women who spontaneously enrolled in the study possibly mitigated this bias. Third, the analyzed sample has a relatively small size. Nevertheless, as shown from the findings of this study, it remains largely representative of the average Mexican female population.

## Conclusion

This study, conducted on a group of voluntary women, largely reflected the epidemiology of osteoporosis in a Mexican female population: the prevalence of osteoporosis assessed by REMS is in line with the values reported in the recent literature, estimated using the conventional DXA. The burden of this disease and its main clinical consequences (i.e., the fragility fracture) has been widely studied. In particular, a Mexican study has shown the imbalance existing between the affected population and availability of bone densitometry devices, with 85% of DXA equipment allocated in private healthcare, resulting accessible only to a minor part of the population [19].

The accuracy of the novel REMS technology has already been assessed in comparison to the gold standard technology, both in terms of diagnosis of osteoporosis [16] and fracture risk prediction [41]. A recently published clinical study, performed at the European level that included a wider age range as well as a larger sample size, confirmed the diagnostic effectiveness of REMS, corroborating the findings of Di Paola and colleagues [42]. Lastly, the high degree of accuracy of REMS for the diagnosis of osteoporosis was demonstrated in comparison with DXA on a multiracial population of Brazilian women [43].



Thereby, substantial scientific evidence suggests that, despite the fact that a rigid training program of the technologist is required to strictly comply with the guidelines in order to maximize the quality of the obtained acquisitions [16], REMS has a beneficial impact in the clinical setting. The utilization of REMS implies several advantages: (i) the non-invasiveness, thanks to the employment of non-ionizing radiation; (ii) the simplicity and rapidity of the examination, due to the guided ultrasound acquisition and the fully automatic result analysis that in turn allows to perform high volumes of examinations; (iii) the portability of the devices and the unnecessary of dedicated infrastructures. Overall these aspects support the employment of this technology in the clinical routine in order to facilitate the early diagnosis of osteoporosis at a population-wide level.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s11657-022-01080-2>.

## Declarations

**Conflicts of interest** None.

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